REMARKS

Status of the Claims

Supplemental to the amendment submitted on July 12, 2011, in response to the January 13, 2011, Office Action and the Advisory Action dated June 1, 2011, the present amendment and remarks are submitted herewith.

Claims 1, 5-9, and 13-22 are pending in the present application. Claims 6, 14, and 18-21 are withdrawn as directed to a non-elected invention. Claims 2-4 and 10-12 were previously canceled. Claims 1 and 9 are amended. Support for the amendments is found throughout the application as originally filed including Example 4, Fig. 1, and Fig. 2.

No new matter is entered by way of this amendment. Reconsideration is respectfully requested.

Issues under 35 U.S.C. § 103(a)

Claims 1, 7-9, 15-17, and 22 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over Kessels *et al.*, *Nature Immunology*, 2:957-961, ("Kessels") in view of Fujio *et al.*, *Journal of Immunology*, 165:528-532, ("Fujio"), Tsuji *et al.*, *Cancer Science*, 2003, 94:389-393, ("Tsuji"), and Nishimura, *Cancer Treatment and Host*, 12:363-373, ("Nishimura").

Claims 1, 5, 9, and 13 are also rejected under 35 U.S.C. § 103(a) as allegedly obvious over Kessels, Fujio, Tsuji, and Nishimura, in view of U.S. Patent No. 7,323,181 to Gaiger *et al.*, ("Gaiger").

The cited references do not teach or suggest all of the elements of the instant claims

Applicants submit that none of the cited references, when considered either alone or in combination, teach or suggest all of the elements in the instant claims. The claims specify that the helper T1 cells are transduced with a MHC class I-restricted T cell receptor gene that recognizes a cancer associated antigen. None of the cited references teach or suggest this feature. For example, Kessels teaches that T cells expressing TCR were obtained after induction with a class I-restricted antigen, but CD4+ cells specific to influenza virus were not obtained. Moreover, neither Fujio, Tsudi, Nishimur,a nor Gaiger remedy the deficiencies of Kessels, *see* Applicants response dated May 12, 2011, and *in particular*, the Table submitted with the May

12, 2011, response describing the differences between the claimed invention and the cited references. Accordingly, the claims are not obvious in view of the cited references.

The specification enables the instant claims

In the Examiner interview summary, which issued on July 29, 2011, the Examiner noted that Applicants may file a supplemental amendment and remarks regarding the enablement of the instant claims. In particular, during the interview, the Examiner suggested that claims 1 and 9 be amended for clarity to specify "wherein the helper T1 cells are activated or proliferated." The Examiner further indicated that he would review the instant application to ensure that the specification supports the present claims.

The claims are amended according to the Examiner's suggestion. Further, Applicants submit that the present claims are enabled by the instant application. The instant claims describe the step of imparting antigen specificity to helper T1 cells (claim 1) or helper T1 cells and cytotoxic T1 cells (claim 9) by transducing the cells with a MHC class I-restricted T cell receptor gene that recognizes a cancer-associated antigen. The resultant helper T1 cells are activated or proliferated. As described further below, support for the present claims is found in the Examples and the Figures.

Activation

The specification supports that the helper T1 cells are activated and proliferated using the steps described in the claimed methods. For example, the activation of the helper T1 cells is described in Example 4 and Fig. 1 of the present application. Activation of helper T1 cells is manifested by cytotoxicity and the production of IFN in a HLA-restricted and antigen specific manner. In particular, Example 4 on page 18 states:

> IFN-γ production was observed for both WT1-A24TCR+Th1 cells and WT1-A24TCR+Tc1 cells co-cultured with WT1 peptide-pulsed LCL cells, but not for those co-cultured with non-peptide-pulsed LCL cells (Fig. 1).

Specifically, antigen-presenting cells (LCL cells) are pulsed with WT-1 peptide and then the antigen-presenting LCL cells are co-cultured with Th1 cells having the MHC class I-restricted T cell receptor gene, resulting in the production of IFN, *see* Fig. 1, leftmost bar.

When Th1 cells, which do not have the MHC class I-restricted T cell receptor gene, are co-cultured with the antigen-presenting LCL cells, no IFN production is observed, *see* Fig. 1, third bar. Moreover, when Th1 cells, which express the MHC class I-restricted T cell receptor gene and LCL cells, which do not present antigen, are co-cultured, no IFN production is observed, *see* Fig. 1, fifth bar.

Proliferation

The helper T1 cells, which are induced according to the claimed methods, produce IL-2. Fig. 2 shows that the genetic transformation and antigen-presentation by LCL cells results in a change in the type of cytokine, which is produced by the cells, that is, from IFN to IL-2. IL-2 is a growth factor for Th1 cells. Thus, this result demonstrates that activated helper T1 cells produce the growth factor, IL-2.

Applicants submit that an ordinary artisan recognizes that IL-2 serves as a growth factor for all types of T cells and that the biological activity of IL-2 is to stimulate differentiation and proliferation of activated T cells. Accordingly, the data depicted in the Examples and Figures of the originally filed application demonstrate that the helper T1 cells are, indeed, activated and proliferated.

In view of the foregoing, an ordinary artisan would have clearly recognized from the present application that the helper T1 cells are activated and proliferated using the claimed methods. Accordingly, the specification enables the instant claims.

CONCLUSION

In view of the above amendment and remarks, Applicants believe that the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Linda T. Parker, Ph.D., Registration No. 46,046, at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

Dated: SEP 15 2011

Respectfully submitted,

Reg. No.

By Linda Parker 46,046

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